REMARKS

A. Introductory Remarks

Applicant respectfully requests reconsideration of this application in view of the following remarks.

Claims 13-24 remain pending in the application, with claim 14 being withdrawn from consideration. No claims are presently being amended, added or canceled.

B. Objection to the Abstract is Obviated by the Substitute Abstract

The Office objected to the abstract for comprising multiple paragraphs.

Applicant submits herewith a revised abstract, which contains a single paragraph of text. Substitution of the revised abstract will obviate the rejection. Applicant therefore requests withdrawal of this ground for objection.

C. Claims 20-22 are Definite, in Accord with 35 U.S.C. § 112, 2nd Paragraph

Claims 20-22 were rejected under 35 U.S.C. § 112, 2nd paragraph, as allegedly being indefinite for using the designation "anti-HM1.24" to identify an antibody. According to the Office, "[l]aboratory designations cannot be held constant outside of the laboratory in which they are used." The Examiner therefore recommended identifying the antibody by depository accession number. Applicant respectfully traverses this rejection.

The B-cell antigen HM1.24 is well known and fully defined. Accordingly, the meaning of the term "anti-HM1.24 antibody" is clear. As early as 1994, HM1.24 was known to be a 29 to 33 kD membrane glycoprotein associated with mature Ig-secreting B cells. See, Goto *et al.*, *Blood* 84(6): 1922-1930 (1994) (already of record). A monoclonal antibody useful for isolating HM1.24 also was known. *Id.* Subsequent to that first report concerning HM1.24, a human cDNA for the antigen was isolated and the glycoprotein's gene structure, including the promoter region, was analyzed. See Ohtomo *et al.*, *Biochem. Biophys. Res. Commun.* 258(3): 583-591 (1999) (abstract attached, full copy to follow). Thus, the HM1.24 antigen is clearly defined outside of Applicant's own laboratory. In view of this clear definition, the term "anti-HM1.24 antibody" has a clear meaning to those skilled in the art as an antibody that specifically binds to HM1.24.

An example of such an antibody is that made by the hybridoma FERM BP-5233, which is on deposit under the provisions of the Budapest Treaty with the National Institute of Bioscience and Human-Technology in Japan. The claims, however, are not limited to this single antibody, as others can readily be manufactured by those of ordinary skill in the art.

Because the meaning of the term "anti-HM1.24 antibody" is clear, Applicant respectfully requests withdrawal of the indefiniteness rejection.

D. The Conditions of the Budapest Treaty Have Been Satisfied

The Office rejected claims 19-22 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not adequately described in the specification. In particular, the Office stated that an HM1.24 antibody is required to practice the claimed invention, and that the antibody must therefore be readily available to the public. Although the specification states that a hybridoma that produces HM1.24 is on deposit under the provisions of the Budapest Treaty, the Office requested a formal declaration to that effect.

In compliance with the Office's request, Applicant submits herewith an executed declaration attesting that a hybridoma, designated FERM BP-5233, that produces an anti-HM1.24 antibody is on deposit under the provisions of the Budapest Treaty. Applicant wishes to emphasize, however, that the claims are not limited to this single antibody. One skilled in the art could readily use the HM1.24 antigen and well-known means to produce other anti-HM1.24 antibodies.

E. Claims 13 and 15-24 are Patentable over the Prior Art

Claims 13 and 15-24 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 5,298,420 ("Chang") in view of Goto *et al.*, *Blood* 84(6): 1922-1930 (1994) ("Goto"). In particular, the Examiner asserted that Chang teaches a method of inhibiting B lymphocyte activation by administering an antibody that binds B cells, and that Goto teaches the use of the HM1.24 antibody, which binds to SEQ ID NO: 1 on terminally differentiated B cells, to treat multiple myeloma. Combining the two references, the Examiner concluded that one skilled in the art would have been motivated to use the HM1.24

antibody to eliminate B cells and treat disease. Applicant respectfully disagrees, and traverses the rejection.

The cited references do not teach what the Office Action asserts. First, Chang does not teach a method of inhibiting B lymphocyte activation by administering an antibody that binds B cells. Rather, Chang describes a method of *killing* B lymphocytes via antibody-dependent cellular cytotoxicity (ADCC).[1]

Second, Goto does not teach the use of HM1.24 antibodies to treat multiple myeloma. Instead, it teaches only that HM1.24 protein "represents a specific marker of late-stage B-cell maturation."[2] Although Goto suggests that HM1.24 "*potentially* serves as a target antigen for immunotherapy of multiple myeloma,"[3] it provides no evidence that HM1.24 actually plays a functional role in multiple myeloma. Significantly, the mere coincidence of HM1.24 expression in mature B-cells does not constitute such evidence.

Because the cited art lacked any specific teaching that HM1.24 plays a functional role in B lymphocyte activation, there was no likelihood of success for practicing the claimed invention prior to filing of the present application. Indeed, it was the present inventor's discovery, that anti-HM1.24 antibody inhibits lymphocyte activation, that made practice of the claimed invention promising. For this reason, the claims are patentable over the cited art, and Applicant respectfully requests withdrawal of the obviousness rejection.

F. Concluding Remarks

The present application is now in condition for allowance, and Applicant respectfully requests favorable reconsideration of it. If the Examiner believes that an interview would advance prosecution, he is invited to contact the undersigned by telephone.

The Commissioner is hereby authorized to charge any additional fees that may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment,

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[1] See col. 6, ll. 45-57; also the Examiner's parenthetical comment on p. 3, 2nd full paragraph of the Office Action.

[2] Pg. 1922, col. 2, ¶ 1.

[3] *Id.*

to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Dec. 22, 2003

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1: Biochem Biophys Res Commun. 1999 May 19;258 (3):583-91.

Molecular cloning and characterization of a surface antigen preferentially overexpressed on multiple myeloma cells.

Ohtomo T, Sugamata Y, Ozaki Y, Ono K, Yoshimura Y, Kawai S, Koishihara Y, Ozaki S, Kosaka M, Hirano T, Tsuchiya M.

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HM1.24 antigen has been identified as a surface molecule preferentially expressed on terminally differentiated B cells, and its overexpression is observed in multiple myeloma cells. The HM1.24 antigen is, therefore, expected as a most potent target molecule for antibody-based immunotherapy for multiple myeloma. Here, we have identified the cDNA for human HM1.24 antigen and also analyzed its gene structure including the promoter region. The HM1.24 antigen is a type II membrane glycoprotein, which has been reported as a bone marrow stromal cell surface antigen BST2, and may exist as a homodimer on myeloma cell surface. Although a reason for the overexpression in myeloma cells is not understood, very interestingly, the promoter region of the HM1.24 gene has a tandem repeat of three cis elements for a transcription factor, STAT3, which mediates interleukin-6 (IL-6) response gene expression. Since IL-6 is a differentiation factor for B cells, and known as a paracrine/autocrine growth factor for multiple myeloma cells, the expression of HM1.24 antigen may be regulated by the activation of STAT3. Importantly, a humanized anti-HM1.24 antibody effectively lysed the CHO transformants which expressed HM1.24 antigen as high as human multiple myeloma cells, but not the cells with lower antigen expression. This evaluation shows that ADCC heavily depends on the expression level of target antigens and, therefore, the immunotherapy targeting the HM1.24 antigen

should have a promising potential in clinical use. Copyright 1999 Academic Press.

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